REMARKS

Upon entry of the present amendments, claims 1-39 will be pending in the present application. Claims 11-16 and 37-39 are under examination and claims 1-10 and 17-36 stand withdrawn (as Applicants with to retain their right to rejoinder). Claim 38 has been amended for added clarity. No new matter has been introduced.

Invention Summary regarding prior grounds for rejection withdrawn: Applicants' representative, Lee Crews, thanks Examiner Barnhart for the courtesy of a telephone call on May 1, 2009. Examiner Barnhart informed the undersigned that she would be supervising Examiner Kosar with respect to the examination of this application and stated that the previous rejections for lack of enablement and clarity would be withdrawn. As stated in the present non-final Office action, "[a]ny rejection and/or objection not specifically addressed is herein withdrawn" (Office action at page 2).

35 U.S.C. § 112, ¶ 2

The Examiner rejected claim 38 for lack of clarity. The Examiner states (Office action at page 2):

> Claim 38 recites the phrase "different mammals, each originating in mice …"' however, it is unclear what the term "each" describes. If Applicant intends for each of the cells to be obtained from a different mammal, wherein each mammal is selected from the group consisting of a mouse, a rat, and ~~or~~ a human, or if some other embodiment is intended, then the claim should so recite.

Applicants appreciate the Examiner's guidance with respect to the claim language, which may have been rendered less clear in the process of translation. Claim 38 has been amended to recite a composition, wherein the hair dermal papilla cells and the active epidermal cells are each obtained from different mammals, wherein the mammal is selected from the group consisting of a mouse, a rat, and a human. Applicants respectfully submit that this amendment obviates the rejection.

35 U.S.C. § 103(a)

Claims 11-16 and 37-39 were rejected on the basis of obviousness over Inamatsu *et al.* (U.S. Patent No. 5,851,831 A; "Inamatsu") in view of Barrandon *et al.* (U.S. Patent No. 4,888,291; "Barrandon"). The Examiner characterizes Inamatsu as teaching "a composition comprising dermal papilla cells cocultured with mammalian epidermal cells" (Office action at page 3, citing Inamatsu at Example 2 and column 4). The Examiner recognizes that Inamatsu fails to suggest "a ratio of papilla cells-to-epidermal cells in the composition and does not exemplify compositions comprising cells each originating from the mammalian species recited in claims 37-39" (Office action at page 3). The Examiner then turns to Barrandon as teaching "that foreskin is a source of epidermal cells …" (Office action at page 4).

In concluding, the Examiner states that "Inamatsu observed a relationship between the proliferation rate of dermal papilla cells and the presence of epidermal cells in culture …" (Office action at page 4, citing Inamatsu at column 4, lines 26-31) and, further, that the present compositions, which require the dermal papilla cells and active epidermal cells to be included at certain ratios, would have been obvious "because Inamatsu teaches a relationship between epidermal cells and the proliferation of ~~an isolated~~ (*sic.*) dermal papilla cells" (Office action at page 4, citing Inamatsu at column 4, lines 24-31). The Examiner argues that (Office action at page 4; emphasis added):

> [O]ne would want to optimize the numbers of the cells in order to optimize this relationship. Accordingly, one would have added *any* amount of epidermal cells to papilla cells with the expectation that a positive proliferation effect would result and wherein success merely requires contacting/combing (*sic.*) the cell species in the composition, which is well with in (*sic.*) the purview of the skilled artisan.

Applicants respectfully disagree with the finding of obviousness. While the compositions now claimed result from mixing a specially made hair dermal papilla cell preparation and active epidermal cells in a ratio "from 1:10 to 10:1" (*see* claim 11), Inamatsu shows absolutely no regard whatsoever for the number of cells used or the ratio of one type with respect to another. Inamatsu does not teach or suggest altering the ratio of the two different cell types, and there is

nothing in Inamatsu that would lead one to think that the outcome might vary depending on the number or ratio of cells within a culture. To the contrary, Inamatsu merely showed that "more favorable results were obtained in terms of both the state of the outgrowth of dermal papilla cells and the proliferation rate thereof, when they are co-cultured with the sole epidermal cells (FIG.1:b) than when they are cultured alone (FIG. 1:a)" (*see* column 4, lines 27-31). This is a binary result based simply on the presence or absence of epidermal cells, not a "relationship" indicating that cell numbers matter or that a particular ratio should be achieved.

With regard to the statement that "one would have added any amount of epidermal cells to papilla cells," the Examiner's attention is kindly directed to Applicants' Example 3, Table 2 (*see* page 20 of the specification as originally filed). Simply supplementing dermal cells with epidermal cells does not necessarily encourage dermal cell growth. It was Applicants' discovery that some ratios were better than others, and nothing in Inamatsu suggested this. Thus, one cannot add *any* amount of epidermal cells to papilla cells and expect a positive proliferation effect. By combining a cell preparation from skin tissue comprising hair dermal papilla cells (the follicular epidermal cells having been killed by cryopreservation) with another cell preparation that contains only (or primarily) epidermal cells as the active cellular component, Applicants discovered the importance of the ratio of these two particular cell types and were able to determine that the more effective ratios of active dermal papilla cells to active epidermal cells for regenerating hair follicles is from 1:10 to 10:1 and preferably from 1:3 to 10:1. This is not suggested by Inamatsu.

One of ordinary skill in the art, upon reading Inamatsu, would also have noticed Inamatsu's teaching regarding conditioned medium. This teaching leads away from the combination of multiple cell types because secreted factors were shown to be effective in activating the outgrowth and proliferation of dermal papilla cells (*see* column 4, lines 31-42). Thus, epidermal cells themselves can be readily omitted. Inamatsu states that "[u]sing this conditioned medium, it becomes possible to subculture pure dermal papilla cells in a stable manner without *any* epidermal cells included, for more than 40 passages" (*see* column 2, lines

52-55; emphasis added in italics). This teaching, at the least, detracts from the motivation one might have otherwise had to modify the ratio of dermal papilla cells to epidermal cells.

The Examiner does not seem to rely much on Barrandon, which discloses that human epidermal cells can be obtained from foreskin (*see* column 3, lines 32-34) and describes the use of these cells as a skin graft on a living non-human animal. The fact that epidermal cells exist in foreskin cannot, however, even in combination with Inamatsu's teaching, suggest the compositions now claimed. Nothing in the cited references, even when combined, suggests that one should modify the specific proportions of hair dermal papilla cells and active epidermal cells in compositions as now claimed. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUDING FORMALITIES

In light of the claims amendments and remarks discussed and made herein, Applicants submit that the pending claims are allowable and request early and favorable action thereon.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 23757-0009US1.

Respectfully submitted,

Date: August 7, 2009

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